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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/540,276	06/21/2005	Anna Ingrid Kristina Berggren	133087.10001(100939-1PUS)	8864

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EXAMINER	
YOUNG, SHAWQUIA	
ART UNIT	**PAPER NUMBER**
1626	

MAIL DATE	DELIVERY MODE
04/30/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/540,276	BERGGREN ET AL.	
	Examiner	Art Unit	
	SHAWQUIA YOUNG	1626	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 February 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *12,14,20 and 27* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *20* is/are allowed.

6)☒ Claim(s) *12,14 and 27* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *2/7/08, 2/7/08*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 12, 14, 20 and 27 are currently pending in the instant application. Applicants have cancelled claim 21 in an amendment filed on February 12, 2008.

I. *Response to Arguments*

Applicant's amendment, filed February 12, 2008, has overcome the rejection of claim 21 under 35 USC 112, second paragraph as being indefinite. The rejection has been withdrawn.

The Examiner has found prior art and 35 USC 112, first paragraph issues, thus the indication that claims 12, 14 and 27 are allowable has been withdrawn.

II. *Information Disclosure Statement*

The information disclosure statement (IDS) submitted on February 7, 2008 is in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statement has been considered by the examiner.

II. *Rejection(s)*

35 USC § 103 - OBVIOUSNESS REJECTION

The following is a quotation of 35 U.S.C. § 103(a) that forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Graham v. John Deere Co. set forth the factual inquiries necessary to determine obviousness under 35 U.S.C. §103(a). *See Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966). Specifically, the analysis must employ the following factual inquiries:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 12, 14 and 27 are rejected under 35 U.S.C. § 103(a) as being unpatentable over *Smith, et al*. (US 2004/0267028). Applicants claim a compound selected from

2-methyl-N, 1,5-triphenyl- 1H-pyrrole-3-carboxamide;

1-(4-chlorophenyl)-2-methyl-N,5-diphenyl-lH-pyrrole-3-carboxamide;

1-(4-methoxyphenyl)-2-methyl-N,5-diphenyl-lH-pyrrole-3-carboxamide;

5-(2,4-dichlorophenyl)-2-methyl-N,l-diphenyl-lH-pyrrole-3-carboxamide;

1-(4-chlorophenyl)-5-(2,4-dichlorophenyl)-2-methyl-N-phenyl-lH-pyrrole-3-carboxamide;

5-(2,4-dichlorophenyl)-l-(4-methoxyphenyl)-2-methyl-N-phenyl-lH-pyrrole-3- carboxamide;

5-(2,4-dimethoxyphenyl)-2-methyl-N,l-diphenyl-lH-pyrrole-3-carboxamide;

1-(4-chlorophenyl)-5-(2,4-dimethoxyphenyl)-2-methyl-N-phenyl-lH-pyrrole-3- carboxamide;

5-(2,4-dimethoxyphenyl)-l-(4-methoxyphenyl)-2-methyl-N-phenyl-lH-pyrrole-3- carboxamide;

2-methyl-l,5-diphenyl-N-piperidin-l-yl-lH-pyrrole-3-carboxamide;

1-(4-chlorophenyl)-2-methyl-5-phenyl-N-piperidin-l-yl-lH-pyrrole-3-carboxamide;

1-(4-methoxyphenyl)-2-methyl-5-phenyl-N-piperidin-1-yl-1H-pyrrole-3-carboxamide;

5 -(2,4-dichlorophenyl)-2-methyl- 1 -phenyl-N-piperidin- 1 -yl- 1H-pyrrole-3 -carboxamide;

1 -(4-chlorophenyl)-5-(2,4-dichlorophenyl)-2-methyl-N-piperidin- 1 -yl- 1H-pyrrole-3- carboxamide;

5-(2,4-dichloropheny1)-1-(4-methoxyphenyl)-2-methyl-N-piperidin-1-yl-1H-pyrrole-3- carboxamide;

1 - { [5 -(2,4-dimethoxyphenyl)-2-methyl- 1 -phenyl- 1H-pyrrol-3 -yl] carbonyl } piperidine;

1-(4-chlorophenyl)-5-(2,4-dimethoxyphenyl)-2-methyl-N-piperidin-1-yl-1H-pyrrole-3- carboxamide;

5-(2,4-dimethoxyphenyl)-1-(4-methoxyphenyl)-2-methyl-N-piperidin-1-yl-1H-pyrrole-3- carboxamide;

1-[(2-methyl-l,5-diphenyl-lH-pyrrol-3-yl)carbonyl]piperidine;

1- {[1-(4-methoxyphenyl)-2-methyl-5-phenyl-lH-pyrrol-3-yl]carbonyl}piperidine; 1 - { [5 -(2,4-dichlorophenyl)-2-methyl- 1 -phenyl- 1H-pyrrol-3 -yl] carbonyl } piperidine; 1 - { [1 -(4-chlorophenyl)-5 -(2,4-dichlorophenyl)-2-methyl- 1H-pyrrol-3 -
yl] carbonyl} piperidine;

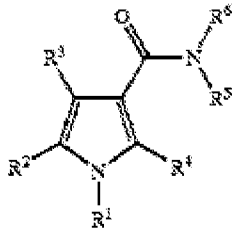
1 - { [5 -(2,4-dichlorophenyl)- 1 -(4-methoxyphenyl)-2-methyl- 1H-pyrrol-3 -
yl] carbonyl} piperidine;

1 - { [1 -(4-chlorophenyl)-5 -(2,4-dimethoxyphenyl)-2-methyl- 1H-pyrrol-3 -
yl] carbonyl} piperidine; and

1 - { [5 -(2,4-dimethoxyphenyl)- 1 -(4-methoxyphenyl)-2-methyl- 1H-pyrrol-3 -
yl] carbonyl} piperidine;

The Scope and Content of the Prior Art (MPEP §2141.01)

Smith, et al. teaches pyrrole derivatives that are used for treating obesity. The invention is represented by the general formula:



Wherein all the variables are as defined in the disclosure (See pages 1-2).

See also preferred embodiments on pages 2-3,

[0031] wherein

[0032] R^1 and R^2 are each a phenyl group optionally substituted with one or more halogen, (C_1-C_6)alkyl, (C_1-C_6)alkoxy, trifluoromethyl, cyano, or nitro;

[0033] R^3 is hydrogen, (C_1-C_6)alkyl, or benzyl; and R^4 is (C_2-C_6)alkyl or NH_2; or

[0034] R^3 is (C_1-C_6)alkyl or benzyl; and R^4 is CH_3;

[0035] R^5 is hydrogen or (C_1-C_6)alkyl;

[0036] R^6 is (C_1-C_6)alkyl, which is optionally substituted with one or more hydroxy, benzyloxy, (C_1-C_6)alkoxy, (C_1-C_6)alkyl-amino, bis[(C_1-C_3)alkyl]-amino, or fluorine,

[0037] benzyl, which is optionally substituted on the phenyl ring with one or more halogen, (C_1-C_6)alkyl, (C_1-C_6)alkoxy, trifluoromethyl, cyano, hydroxy, benzyloxy, or nitro,

[0038] phenyl substituted with one or more (C_1-C_6)alkyl, (C_1-C_6)alkoxy, trifluoromethyl, cyano, hydroxy, benzyloxy, nitro, or halogen,

[0039] piperidin-4-yl, piperidin-3-yl, or pyrrolidin-3-yl, each of which may be optionally substituted on the nitrogen atom of the piperidine or pyrrolidine ring with (C_1-C_6)alkyl, hydroxy-substituted (C_1-C_6)alkyl, or a benzyl or phenyl group that is optionally substituted on the phenyl ring with one or more (C_1-C_6)alkyl, (C_1-C_6)alkoxy, trifluoromethyl, cyano, hydroxy, or halogen,

[0040] —NR^7R^8

[0041] where R^7 is hydrogen or (C_1-C_6)alkyl;

[0042] R^8 is (C_2-C_6)alkyl, or a phenyl group that is optionally substituted with one or more (C_1-C_6)alkyl, (C_1-C_6)alkoxy, hydroxy-substituted (C_1-C_6)alkyl, hydroxy, trifluoromethyl, cyano, nitro, or halogen; or

[0043] R^7 and R^8, taken together with the nitrogen atom to which they are attached, form a 5- to 10-membered saturated heterocyclic radical

which is optionally substituted by one or more $(C_1$-$C_6)$alkyl, $(C_1$-$C_6)$alkoxy, hydroxy-substituted $(C_1$-$C_3)$alkyl, benzyl, phenyl, hydroxy, or fluorine; or

[0044] R^5 and R^6, taken together with the nitrogen atom to which they are attached, form a 5- to 10-membered saturated heterocyclic radical, optionally substituted with one or more $(C_1$-$C_6)$alkyl, $(C_1$-$C_6)$alkoxy, hydroxy, trifluoromethyl, fluorine, or a benzyl or phenyl group that is optionally substituted on the phenyl ring with one or more $(C_1$-$C_6)$alkyl, hydroxy, $(C_1$-$C_6)$alkoxy, trifluoromethyl, cyano, nitro, or halogen.

. Note that R_1 and R_2 are each a phenyl group optionally substituted with one or more halogen, $(C_1$-$C_6)$alkyl, $(C_1$-$C_6)$alkoxy, trifluoromethyl, cyano or nitro (See page 2, paragraph 0032). The prior art reference teaches the species 1-(2-chlorophenyl)-5-(4-methoxyphenyl)-2-methyl-N-(1-piperidinyl)-1H-pyrrole-3-carboxamide (page 7, paragraph 0111).

The Difference Between the Prior Art and the Claims (MPEP §2141.02)

The difference between the prior art of *Smith, et al*. and the instant invention is that there is homologous subject matter. Not all of the substituents are taught, however there is overlap between the species disclosed in the instant claims and species disclosed in the prior art especially in view of the preferred embodiments taught by the prior art. For example, the instant application discloses a species of compound wherein the phenyl ring at the 5-position of pyrrole moiety has dimethoxy substituents versus the phenyl ring having one methoxy substituent as seen in the prior art. See *In re Lemin* 141 USPQ 814- choosing some among many.

Prima Facie Obviousness-The Rational and Motivation (MPEP §2142-2413)

Applicants are claiming various species such as 1-(4-chlorophenyl)-5-(2,4-

dimethoxyphenyl)-2-methyl-N-piperidin-1-yl-1H-pyrrole-3-carboxamide. The prior art reference of *Smith, et al.* teaches a similar compound wherein there is only one methoxy group substituted on the phenyl ring at the 5-position of the pyrrole moiety (See Example 4, page 7). The prior art reference also teaches that the phenyl rings can be substituted by one or more halogen, alkyl, alkoxy, trifluoromethyl, hydroxyl, cyano or nitro. Therefore, it would have been obvious to substitute the phenyl ring with a second methoxy group based on the teachings of the prior art.

In In re Hass, 141 F.2d 127, 60 USPQ 548 (CCPA 1944), it was well established that members of a homologous series must possess unexpected properties not possessed by the homologous compounds disclosed by the prior art. For example, it is obvious to prepare a disubstituted phenyl group (i.e. two methoxy groups) when the art teaches a monosubstituted phenyl group that could be further substituted with a reasonable expectation of success. Specifically, a methoxy substituted phenyl ring and a dimethoxy substituted phenyl ring are considered homologues and are obvious absent unexpected results, especially when the art teaches that the phenyl ring can be further substituted with other substituents such as a methoxy group. Therefore, it would have been prima facie obvious to one having ordinary skill in the art at the time the invention was made to prepare adjacent homologs based on the teachings of the preferred embodiments in the prior art. A strong prima facie obviousness has been established.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 12, 14 and 27 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the compounds listed in claim 12 or stereoisomers, tautomers, racemates or pharmaceutically acceptable salts of said compounds does not reasonably provide enablement for a **solvate** of said compounds. The specification does not provide sufficient guidance nor does it enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

As stated in the MPEP 2164.01 (a), "There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue."

In *In re Wands*, 8 USPQ2d 1400 (1988), factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. 112, first paragraph, have need described. They are:

1. the nature of the invention,
2. the state of the prior art,
3. the predictability or lack thereof in the art,
4. the amount of direction or guidance present,
5. the presence or absence of working examples,
6. the breadth of the claims,
7. the quantity of experimentation needed, and
8. the level of the skill in the art.

In the instant case

The nature of the invention

The nature of the invention is a compound listed in claim 12, or stereoisomers, tautomers and racemates of said compounds, or a pharmaceutically acceptable salt of said compounds. There is no teaching of solvates of the compounds listed in claim 12 in the specification.

The state of the prior art and predictability or lack thereof in the art

It is the state of the prior art that the term "solvate" found in the claims is defined as a compound formed by solvation (the combination of solvent molecules with molecules or ions of the solute. It has been estimated that approximately one-third of the pharmaceutically active substances are capable of forming crystalline hydrates. Predicting the formation of solvates or hydrates of a compound and the number of molecules of water or solvent incorporated into the crystal lattice of a compound is complex and difficult. Each solid compound responds uniquely to the possible formation of solvates or hydrates and hence generalizations cannot be made for a series of related compound (See *Vippagunta, et al.*)

The scope of "solvate" is not adequately enabled or defined. Applicants provide no guidance as how the compounds are made more active *in vivo*. Solvates and hydrates cannot always be predicted and therefore are not capable of being claimed if the applicant cannot properly enable a particular hydrate or solvate.

The amount of direction or guidance present and the presence or absence of working examples

There is no direction or guidance present in the specification or working examples present in the specification are that defines or relates to what solvates are being included in the elected invention.

The breadth of the claims

The breadth of the claims is a compound listed in claim 12, or stereoisomers, tautomers and racemates of said compounds, or a pharmaceutically acceptable salt of said compounds.

The quantity of experimentation needed and the level of the skill in the art

While the level of the skill in the pharmaceutical art is high, the quantity of experimentation needed is undue experimentation. One of skill in the art would need to prepare compounds with various solvents without any direction as to what compounds form solvates with which solvents.

The level of skill in the art is high without showing or guidance as to how to make solvates of the compounds listed in claim 12 it would require undue experimentation to figure out the solvents, temperatures and reaction times that would provide solvates of the above compounds.

To overcome this objection, Applicant should submit an amendment deleting the term “solvates”.

III. *Conclusion*

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shawquia Young whose telephone number is 571-272-9043. The examiner can normally be reached on 5:30 AM-2:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph McKane can be reached on 571-272-0699. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Shawquia Young/

Examiner, Art Unit 1626

/Kamal A Saeed, Ph.D./

Primary Examiner, Art Unit 1626